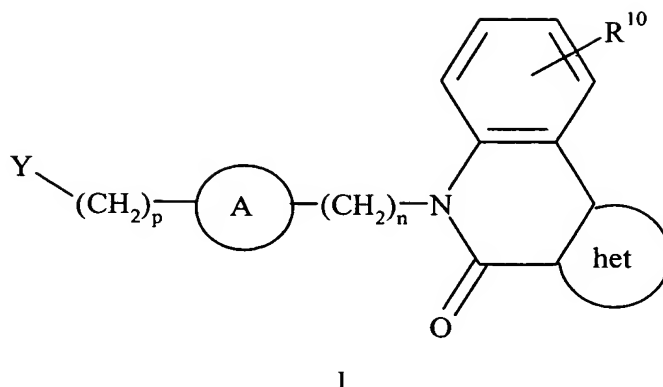


Listing of Claims

1. (currently amended) A compound of formula I:



where:

A is a C₃-C₈ cycloalkyl, optionally substituted 1-3 times with a C₁-C₄ alkyl;

het is a five (5) membered heterocyclic ring comprising N and a second heteroatom selected from N, O, or S;

wherein the non-fused carbon atom of the ~~heteroaryl~~ heterocyclic ring may be optionally substituted with R^b; wherein R^b is C₁-C₆ alkyl, optionally substituted aryl, optionally substituted heterocycle, an amino acid ester, CH₂OH, CH₂O-heterocycle, halo, CH₂N₃, CH₂SR¹, CH₂NR⁴R⁶, OR¹, SR¹³, S(CH₂)_k-phenyl, or NR⁴R⁶; provided that when het is pyrazole or imidazole, the saturated nitrogen of the het ring may be optionally substituted with R^a; wherein R^a is C₁-C₄ alkyl;

k is 0, 1, 2, 3, or 4;

n is 0, 1, or 2;

p is 0 or 1;

q is 0, 1, or 2;

r is 0, 1, or 2;

t is 0, 1, 2, 3, or 4;

u is 0, 1, 2, 3, or 4;

Y is $-E-C(O)R^{13}$, $-E-CH=CHR^{13}$, $-E-C(OH)R^{13}$, $-E-NR^4R^5$, $-E-OR^2$, $-E-S(O)_qR^{13}$, $-E-SO_2NR^4R^6$, $-C(R^{11})=NR^6$, or an optionally substituted heterocycle;

E is a bond or -C(R¹¹)(R¹¹)-;


R¹ is independently at each occurrence hydrogen or C₁-C₆ alkyl;

R² is independently at each occurrence hydrogen, C₁-C₆ alkyl, optionally substituted C₃-C₈ cycloalkyl, optionally substituted (C₁-C₄ alkyl)-aryl, optionally substituted aryl, optionally substituted heterocycle, C(O)-aryl, C(O)N-phenyl, or (CH₂)₂NR⁴R⁵;

R³ is independently at each occurrence hydrogen, C₁-C₆ alkyl, optionally substituted C₃-C₈ cycloalkyl, optionally substituted (C₁-C₄ alkyl)-aryl, optionally substituted aryl, optionally substituted heterocycle, OR¹³, or NR⁴R⁶;

R⁴ is independently at each occurrence hydrogen, C₁-C₆ alkyl, optionally substituted (C₁-C₆ alkyl)-aryl, SO₂CH₃, or optionally substituted aryl; or ~~R⁴ and~~ R⁵, R⁶, or R^{6'} combine with R⁴ to form =CR¹R¹⁴;

R⁵ is independently at each occurrence hydrogen, C₁-C₆ alkyl, C₁-C₄ alkoxy, optionally substituted heterocycle, optionally substituted C₃-C₈ cycloalkyl, optionally substituted C₆-C₁₀ bicycloalkyl, optionally substituted (C₁-C₄ alkyl)-aryl, optionally substituted aryl, optionally substituted (C₁-C₄ alkyl)-heterocycle, C(O)C(O)R¹³, C(O)R⁷,

CH₂R⁷, SO₂R⁸, or a moiety of the formula ; or R⁴ and R⁵, together with the nitrogen to which they are attached, combine to form an optionally substituted N-heterocycle;

R⁶ is independently at each occurrence hydrogen, C₁-C₆ alkyl, C₁-C₄ alkoxy, optionally substituted C₃-C₈ cycloalkyl, optionally substituted C₆-C₁₀ bicycloalkyl, optionally substituted (C₁-C₄ alkyl)-aryl, optionally substituted aryl, optionally substituted (C₁-C₄ alkyl)-heterocycle, or optionally substituted heterocycle; or R⁴ and R⁶, together with the nitrogen to which they are attached, combine to form an optionally substituted N-heterocycle;

R^{6'} is independently at each occurrence hydrogen, C₁-C₆ alkyl, C₁-C₄ alkoxy, optionally substituted C₃-C₈ cycloalkyl, optionally substituted C₆-C₁₀ bicycloalkyl, optionally substituted (C₁-C₄ alkyl)-aryl, optionally substituted aryl, optionally substituted (C₁-C₄ alkyl)-heterocycle, optionally substituted heterocycle, (C₁-C₄ alkyl)-OR¹³:

wherein the (C₁-C₄ alkyl) of the (C₁-C₄ alkyl)-OR¹³ may be optionally substituted from 1 to 2 times with C₁-C₄ alkyl, optionally substituted aryl, or optionally substituted heterocycle;

or R⁴ and R^{6'}, together with the nitrogen to which they are attached, combine to form an optionally substituted N-heterocycle;

R⁷ is independently at each occurrence optionally substituted C₁-C₆ alkyl, C₁-C₆ alkoxy, (C₁-C₄ alkoxy)-aryl, (C₁-C₄ alkoxy)-heterocycle, (C₁-C₄ alkoxy)-Si(CH₃)₃, optionally substituted (C₃-C₈ cycloalkyl), optionally substituted (C₁-C₄ alkyl)-(C₃-C₈ cycloalkyl), optionally substituted (C₁-C₄ alkyl)-aryl, optionally substituted aryl, diphenylmethyl, optionally substituted (C₁-C₄ alkyl)-CO-aryl, optionally substituted CO-aryl, optionally substituted (C₁-C₄ alkyl)-heterocycle, 3-oxo-indanyl, fluoren-9-yl substituted with hydroxy, optionally substituted CH=CH-heterocycle, optionally substituted phenoxy, optionally substituted heterocycle, optionally substituted (C₁-C₄ alkyl)-phenoxy, (CH₂)_tS(O)_rR¹, (CH₂)_tC(R¹²)(R⁹)N(R¹⁶)(R¹⁵), (CH₂)_tC(R¹²)(R⁹)O(R¹⁷), (CH₂)_tC(R¹²)(R⁹)S(R¹⁷), or NR⁴R^{6'};

R⁸ is independently at each occurrence optionally substituted C₁-C₆ alkyl, optionally substituted aryl, optionally substituted (C₁-C₄ alkyl)-aryl, optionally substituted (C₁-C₄ alkyl)-heterocycle, or optionally substituted heterocycle;

R⁹ is independently at each occurrence hydrogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₈ cycloalkyl, optionally substituted (C₁-C₄ alkyl)-aryl, optionally substituted aryl, optionally substituted heterocycle, (CH₂)_u-(C₁-C₆ alkoxy), optionally substituted (CH₂)_u-O-(C₃-C₈ cycloalkyl), optionally substituted (CH₂)_u-(C₁-C₄ alkoxy)-aryl, optionally substituted (CH₂)_u-O-aryl, optionally substituted (CH₂)_u-O-heterocycle, (C₁-C₄ alkyl)-CO₂-(C₁-C₆ alkyl), optionally substituted (C₁-C₄ alkyl)-CO₂-(C₃-C₈ cycloalkyl), optionally substituted (C₁-C₄ alkyl)-CO₂-(C₁-C₄ alkyl)-aryl, optionally substituted (C₁-C₄ alkyl)-CO₂-aryl, or optionally substituted (C₁-C₄ alkyl)-CO₂-heterocycle; or R⁹ and R¹² combine to form a C₃-C₈ cycloalkyl;

R¹⁰ is 0 to 4 substituents from the aryl ring independently at each occurrence hydrogen, halo, C(O)R³, cyano, optionally substituted heterocycle, optionally substituted aryl, C≡C-R¹, C₁-C₄ alkoxy, (C₁-C₄ alkyl)-phenyl, NR¹⁹R²⁰, CH₂OH, CO₂CH₂CO₂CH₂CH₃, or C₂-C₆ alkenyl;

R¹¹ is independently at each occurrence hydrogen, C₁-C₆ alkyl, optionally substituted heterocycle, optionally substituted (C₁-C₄ alkyl)-heterocycle, optionally substituted aryl, or optionally substituted (C₁-C₄ alkyl)-aryl;

R¹² is independently at each occurrence hydrogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₈ cycloalkyl, optionally substituted (C₁-C₄ alkyl)-aryl, optionally substituted aryl, optionally substituted (C₁-C₄ alkyl)-heterocycle or optionally substituted heterocycle;

R¹³ is independently at each occurrence hydrogen, optionally substituted C₁-C₆ alkyl, methoxy, hydroxy, optionally substituted C₃-C₈ cycloalkyl, optionally substituted (C₁-C₄ alkyl)-aryl, optionally substituted aryl, CO₂CH₂CO₂CH₂CH₃, or optionally substituted heterocycle;

R¹⁴ is independently at each occurrence C₁-C₆ alkyl or optionally substituted (C₁-C₄ alkyl)-aryl;

R¹⁵ is independently at each occurrence hydrogen, C₁-C₆ alkyl, optionally substituted C₃-C₈ cycloalkyl, optionally substituted C₆-C₁₀ bicycloalkyl, optionally substituted (C₁-C₄ alkyl)-aryl, optionally substituted aryl, optionally substituted (C₁-C₄ alkyl)-heterocycle, optionally substituted heterocycle, C(O)OR¹³, SO₂R⁸, C(O)R¹⁸, or a

moiety of the formula $\begin{array}{c} \text{S} \\ | \\ \text{---} \text{NHR}^8 \end{array}$;

R¹⁶ is independently at each occurrence hydrogen, optionally substituted C₁-C₆ alkyl, optionally substituted aryl, optionally substituted heterocycle, SO₂CH₃ or -COR⁸; or R¹⁶ and R¹⁵, together with the nitrogen to which they are attached, combine to form an optionally substituted N-heterocycle;

R¹⁷ is independently at each occurrence hydrogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₈ cycloalkyl, optionally substituted (C₁-C₄ alkyl)-aryl, optionally substituted aryl, COR¹⁸, optionally substituted heterocycle, optionally substituted (C₁-C₄ alkyl)-heterocycle, optionally substituted C₁-C₆ alkoxy, optionally substituted (C₁-C₄ alkoxy)-aryl, optionally substituted (C₁-C₄ alkoxy)-heterocycle, (C₁-C₄ alkyl)-N(R¹)(R¹), or an amino acid ester;

R¹⁸ is independently at each occurrence hydrogen, optionally substituted C₁-C₆ alkyl, optionally substituted C₃-C₈ cycloalkyl, optionally substituted (C₁-C₄ alkyl)-aryl, optionally substituted aryl, optionally substituted heterocycle, (C₁-C₄ alkyl)-NHCO₂-(C₁-C₄ alkyl), or optionally substituted (C₁-C₄ alkyl)-heterocycle;

R¹⁹ is independently at each occurrence hydrogen, CO-(C₁-C₄ alkyl), or optionally substituted C₁-C₆ alkyl;

R²⁰ is independently at each occurrence hydrogen, optionally substituted C₁-C₆ alkyl, CH₂OH, or CO-(C₁-C₄ alkyl);

or a pharmaceutical salt thereof;

wherein:

optionally substituted C₁-C₄ alkyl and optionally substituted C₁-C₆ alkyl refers to a C₁-C₄ alkyl or C₁-C₆ alkyl, respectively, unsubstituted or substituted from 1 to 3 times with halo, C₁-C₄ alkanol, NH₂, or hydroxy;

optionally substituted C₃-C₈ cycloalkyl refers to a C₃-C₈ cycloalkyl unsubstituted or substituted once with a phenyl, substituted phenyl, hydroxy, or CO₂R¹ group;

optionally substituted (C₁-C₄ alkyl)-(C₃-C₈ cycloalkyl) refers to optionally substituted C₃-C₈ cycloalkyl linked through an optionally substituted C₁-C₄ alkyl;

optionally substituted O-(C₃-C₈ cycloalkyl) refers to an optionally substituted C₃-C₈ cycloalkyl linked through an oxygen atom;

optionally substituted C₆-C₁₀ bicycloalkyl refers to a C₆-C₁₀ bicycloalkyl unsubstituted or substituted once with a phenyl, substituted phenyl, or CO₂R¹ group;

optionally substituted aryl refers to a phenyl and naphthyl group, respectively, unsubstituted or substituted from 1 to 5 times independently with C₁-C₆ alkyl, halo, hydroxy, trifluoromethyl, phenyl, phenoxy, SO₂R¹, OR¹¹, NR⁴R⁵, SO₂N(R¹³)₂, NH-Pg, C₁-C₆ alkoxy, benzyloxy, C(O)R¹³, C₅-C₇ cycloalkyl, trifluoromethoxy, SR¹, cyano, or nitro;

optionally substituted (C₁-C₄ alkyl)-aryl refers to optionally substituted aryl linked through an optionally substituted C₁-C₄ alkyl;

optionally substituted O-aryl refers to an optionally substituted aryl linked through an oxygen atom;

optionally substituted phenoxy refers to a phenoxy group unsubstituted or substituted from 1 to 3 times independently with C₁-C₆ alkyl, halo, hydroxy, trifluoromethyl, NR⁴R⁶, SO₂N(R¹³)₂, NH-Pg, C₁-C₆ alkoxy, benzyloxy, C(O)R¹³, C₅-C₇ cycloalkyl, trifluoromethoxy, cyano, or nitro;

optionally substituted (C₁-C₄ alkyl)-phenoxy refers to unsubstituted or substituted phenoxy linked through an optionally substituted C₁-C₄ alkyl;

heterocycle is taken to mean stable unsaturated and saturated 3 to 6 membered rings containing from 1 to 4 heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur, said rings being optionally benzofused. All of these rings may be substituted with up to three substituents independently selected from the group consisting of halo, C₁-C₄ alkoxy, C₁-C₄ alkyl, cyano, nitro, hydroxy, -S(O)_m-(C₁-C₄ alkyl) and -S(O)_m-phenyl where m is 0, 1 or 2;

optionally substituted heterocycle refers to a heterocyclic ring unsubstituted or substituted 1 or 3 times independently with a C₁-C₆ alkyl, halo, benzyl, optionally substituted phenyl, SR¹, C₁-C₄ alkoxy, CO₂R¹, nitro, cyano, (C₁-C₄ alkyl)-cyano, heterocycle, NR¹⁹R²⁰, COR¹², C₁-C₆ alkanol, benzyloxy, phenoxy, trifluoromethyl. Heterocyclic rings may be additionally substituted 1 or 2 times with an oxo group;

optionally substituted O-heterocycle refers to an optionally substituted heterocycle linked through an oxygen atom;

optionally substituted (C₁-C₄ alkyl)-heterocycle refers to optionally substituted heterocycle linked through an optionally substituted C₁-C₄ alkyl;

N-heterocycle refers to a nitrogen containing heterocycle linked through a nitrogen atom; and

optionally substituted N-heterocycle refers to a N-heterocycle, optionally substituted 1 or 3 times independently with a C₁-C₆ alkyl, halo, benzyl, optionally substituted phenyl, SR¹, C₁-C₄ alkoxy, CO₂R¹, nitro, cyano, (C₁-C₄ alkyl)-cyano, heterocycle, NR¹⁹R²⁰, COR¹², C₁-C₆ alkanol, benzyloxy, phenoxy, trifluoromethyl; and additionally substituted 1 or 2 times with an oxo group.

Claims 2-3 (canceled)

Claim 4. (currently amended) The compound of ~~any one of Claims 1-3~~ Claim 1 where A is 1,3-cyclohexyl.

Claims 5-18 (canceled)

Claim 19. (original) A method of inhibiting MRP1 in a mammal which comprises administering to a mammal in need thereof an amount effective to inhibit MRP1 of a compound of formula I, as defined in Claim 1, or a pharmaceutical salt thereof.

Claims 20-58 (canceled)

Claim 59. (original) A pharmaceutical formulation comprising a compound of formula I, as defined in Claim 1, or a pharmaceutical salt thereof; in combination with one or more pharmaceutical carriers, diluents, or excipients therefor.

Claims 60-65 (canceled)

Claim 66. (original) A pharmaceutical composition for inhibiting MRP1 in a mammal which comprises an effective amount of a compound of formula I, as defined in Claim 1, or a pharmaceutical salt thereof.

Claims 67-71 (canceled)

72. (new) The compound of Claim 1 which is (3-[[5-(2-Chloro-6-fluoro-phenyl)-3-methyl-3H-imidazole-4-carbonyl]-amino]-cyclohexylmethyl)-carbamic acid benzyl ester.

73. (new) The compound of Claim 1 which is (3-(9-Chloro-3-methyl-4-oxo-3,4-dihydro-imidazole-[4,5-c]-quinolin-5-yl)-cyclohexylmethyl)-benzamide.

74. (new) The compound of Claim 1 which is (3-(9-Chloro-3-methyl-4-oxo-3,4-dihydro-imidazole-[4,5-c]-quinolin-5-yl)-cyclohexylmethyl)-carbamic acid benzyl ester.

75. (new) The compound of Claim 1 which is N-[3-(9-Chloro-3-methyl-4-oxo-2,4-dihydropyrazolo[4,3-c]quinolin-5-yl)-cyclohexylmethyl]benzamide.

76. (new) The compound of Claim 1 which is N-[3-(9-Chloro-3-methyl-4-oxo-2,4-dihydropyrazolo[4,3-c]quinolin-5-yl)-cyclohexylmethyl]-6-fluoronicotinamide

77. (new) The compound of Claim 1 which is N-[3-(4,10-Dichloro-5-oxo-5H-benzo[h] [1,6]naphthyridin-6-yl)-cyclohexylmethyl]-benzamide.

78. (new) The compound of Claim 1 which is N-[3-(10-Chloro-4-methoxy-5-oxo-5H-benzo[h] [1,6]naphthyridin-6-yl)-cyclohexylmethyl]-benzamide.

79. (new) The compound of Claim 1 which is N-[3-(10-Chloro-4-methylamino-5-oxo-5H-benzo[h] [1,6]naphthyridin-6-yl)-cyclohexylmethyl]-benzamide.